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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/626,616	07/27/00	YU L	INDA:005USD1

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1647	3

DATE MAILED: 12/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/626,616	YU, LEI	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-47 and 65-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-47 and 65-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Preamendment A, filed 7/27/00, has been entered into the record.

B. Claims 1-64 were pending in the application. Claims 1-43 and 48-64 were cancelled and claims 65-83 have been added. However, claim 66 cannot be found. Therefore, claims 67-83 have been renumbered under 37 CFR 1.126 as claims 66-82. Claims 44-47 and 65-82 are currently pending.

2. Brief Description of Drawings

A. The Brief Description of the Drawings is objected to. Figure 1 has 2 parts to the figure, A and B. However, this is not referred to in the Brief Description of Drawings. Furthermore, Figures 2, 5, 6, 7, 8, 11, 18, 19, 20, 21, 23 and 24 have more than one drawing associated with them and needed to be labeled as such before the drawing is described. For example, "**FIG. 2A-B**. Panels A and B..." Appropriate correction is required.

3. Claim Objections

A. Claim 72 (renumbered) is objected to since part (iii) should recite "ability of the candidate substance to activate ion channels..."

B. Claim 75 (renumbered) is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 74 (renumbered). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim

75 recites that the nucleic acid sequence needs to contain guanine at position 389 of SEQ ID NO:7, which has already been recited in claim 74 (a).

C. Claim 75 (renumbered) is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 75 recites that the nucleic acid sequence needs to contain guanine at position 389 of SEQ ID NO:7, which has already been recited in renumbered claim 74 (a).

4. Claim Rejections - 35 USC § 112, first paragraph – lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 44-47 are genus claims. Applicants have only provided an adequate written description of the mu opioid receptor of SEQ ID NO:2, 4, 8 and 17. The term "mu opioid receptor" would encompass proteins having one or more amino acid substitutions, deletions, insertions and/or additions to SEQ ID NO:2, 4, 8 or 17. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since

the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:2, 4, 8 and 17 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

In addition, claim 44 is rejected since there is a lack of adequate written description of the term "interact." Applicants have not adequately described all of the possible interactions of a candidate substance with the mu opioid receptor of the invention. For example, the term "interact" can refer to a compound which has a direct interaction with the receptor, such as binding, or the term could refer to a compound which interacts indirectly with the claimed receptor.

B. Claims 65, 66-70, 73-80 and 82 (all but 65 renumbered) are genus claims. The claims recite a process of using a mu opioid receptor encoded for by nucleic acid sequences which comprise at least 35-100 nucleotides of SEQ ID NO:7. However, there is no written description with regards to knowing the function of these fragments. Furthermore, not only would these nucleic acid sequences of, for example, 35 contiguous nucleotides of SEQ ID NO:7 not encode the full length receptor, but there is no written description as to what these fragments would encode. These nucleic acids could encode a protein having one or more amino acid substitutions, deletions, insertions and/or additions to SEQ ID NO:7. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid alterations that can be made to SEQ ID NO:7. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish

compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, fragments of at least 35-100 nucleic acids of SEQ ID NO:7 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made. Claims 74, 76 and 83 are rejected since they depend from rejected base claims. Claims 72 and 82 are objected to since they depend from rejected base claims.

5. Claim Rejections - 35 USC § 112, first paragraph – scope

A. Claims 44-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the mu opioid receptors of SEQ ID NO:2, 4, 8 and 17, does not reasonably provide enablement for all mu opioid receptors, or for peptides encoded for by at least 35-100 nucleic acids of SEQ ID NO:7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is too large with regard to the phrase "mu opioid receptor." This would allow Applicants rights to all mu opioid receptors from all species of mammals since there is a lack

of both guidance and working examples in the claims and in the specification as to how one of ordinary skill in the art would be able to differentiate a mu opioid receptor from other opioid receptors. Given the lack of guidance in the claims and in the specification as to what constitutes a mu opioid receptor and what separates these receptors from other opioid receptors, it is not predictable to one of ordinary skill in the art how to make a mu opioid receptor of the invention.

In addition, these claims discuss a method of identifying a compound which interacts with a peptide encoded for by at least 35-100 contiguous nucleotides of SEQ ID NO:7. However, Applicants give no guidance in determining which peptide fragments encoded for by at least 35-100 nucleotides of SEQ ID NO:7 are capable of interacting with a compound. This lack of written description of how to determine which fragments are capable of interacting with a compound leads to a lack of enablement in producing ligand binding fragments of SEQ ID NO:7. In addition, Applicants have provided no guidance or working examples of how to make a mu opioid receptor which consists of as few as 35 nucleotides of SEQ ID NO:7, nor is it predictable to one of ordinary skill in the art how to make a functional mu opioid receptor encoded by as few as 35 nucleotides of SEQ ID NO:7.

In summary, the breadth of the claims is too large with regard to all mu opioid receptors of all species. In addition, there is a lack of guidance and working examples which allows one to differentiate mu opioid receptors from other opioid receptors as well as how to make a functional mu opioid receptor consisting of as few as 35 nucleic acids of SEQ ID NO:7. There is also a lack of predictability with regard to how to make all mu opioid receptors claimed by the invention, or how to make a functional mu opioid receptor encoded by as few as 35 nucleotides of SEQ ID NO:7. For these reasons, the Examiner holds that undue experimentation is necessary to make the claimed mu opioid receptors.

6. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 44-47 are vague and indefinite in reference to the term "mu opioid receptor." Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "mu opioid receptor" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

B. Claim 44 is rendered vague and indefinite because of the term "interact." It is not clear from the claims or the specification what this term refers to. The interaction could be, for example, the compound binding to the receptor, which could include water, or an indirect interaction in which the compound binds to or activates a mechanism downstream from the claimed opioid receptor. Claims 45-47 are objected to since they depend from rejected claim 44.

C. Claim 73 is rendered vague and indefinite because part (i) of the claim recites the phrase "binding ability." It is not clear what this phrase means. First, it is unclear if the claim is measuring the binding ability of the candidate substance or of the receptor. In addition, it is not clear what either of these molecules is binding to.

This claim is also confusing since part (iv) recites "...in the cell membrane." It is not clear that the cell membrane comprises the claimed recombinant opioid receptor polypeptide. This part of the claim could be made more clear by reciting "...in the cell membrane of part (iii)."

7. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 44-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins et al. Hawkins et al. teach a process of screening a candidate substance for its ability to interact with a mu opioid receptor by providing a mu opioid receptor polypeptide, a candidate substance and measuring the binding affinity of the ligand for the receptor (see, for example, the Abstract, Figure 3 and paragraph 7 under "Results"). Though the reference does not specifically teach a process for determining the intrinsic activation ability of the candidate substance for the receptor, Tables 4a-c teach the binding affinity for numerous mu opioid agonists and antagonists. The teaching that these compounds are mu *agonists and antagonists* implies that these compounds have intrinsic activity at the mu receptor. In addition to this teaching, one of ordinary skill in the art would immediately envision that the binding data presented in these Tables also shows that these mu agonists and antagonists have intrinsic activation ability since they are able to bind to these mu receptors and, therefore, have an intrinsic activation ability, even if this ability is determined to be zero.

B. Claims 44-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Kennedy et al. Kennedy et al. teach a process of screening a candidate substance for its ability to interact with a mu opioid receptor by providing a mu opioid receptor polypeptide, a candidate substance and determining the intrinsic activation ability of this substance (Abstract; Figure 1, 2 and 3). Kennedy et al. also teach the binding of the candidate substance for the receptor since the inhibition of morphine-induced I_{ca} inhibition is reversed by the opioid-specific antagonist, naloxone (Figure 1). Therefore, since mu opioid receptors

are the only opioid receptors present in these neuroblastoma cells, then the inhibition of the effects of morphine demonstrate that morphine binds the mu opioid receptor.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
December 01, 2000

Gary L. Kunz

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